PATENT--FEE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:

WILLIAM ERNEST PULLMAN ET AL.

Serial No.: 10/031,556

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I hereby certify that this paper is being deposited with the United States Postal Service with sufficient postage, as first class mail, in an envelope addressed to:
Commissioner for Patent
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DECLARATION OF DR. GREGORY D. SIDES, M.D., F.A.C.E.P., F.A.C.P.
UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

NOW COMES Dr. Gregory D. Sides, Declarant herein, and states as follows:

1. I presently hold the position of Medical Director, Primary Care Products, Cialis® Product Team at Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285.

2. My previous positions were:

Director, Bioproduct Medical, Eli Lilly and Company, Indianapolis, Indiana (Jan 2002 - Jan 2003)

Director of Operations, Global Clinical Research, Eli Lilly and Company, Indianapolis, Indiana (Feb 2001 - Jan 2002)

Acting Director, Cardiovascular Medical, Eli Lilly and Company, Indianapolis, Indiana (Jul 2000 - Feb 2001)

Senior Clinical Research Physician, Cardiovascular, Medical, Eli Lilly and Company, Indianapolis, Indiana (Jan 1999 - Jul 2000)

Clinical Research Physician, Cardiovascular Division, Eli Lilly and Company, Indianapolis, Indiana (Jul 1994 - Dec 1998)

Clinical Research Physician, Infectious Diseases Division, Eli Lilly and Company, Indianapolis, Indiana (Mar 1990 - Jul 1994)

Associate Clinical Research Physician, Infectious Diseases Division, Eli Lilly and Company, Indianapolis, Indiana (Feb 1988 - Mar 1990)

Partner, Kirtley, Paschall, Sides Emergency Physicians, Inc., Danville, Indiana (Nov 1984 - Mar 1988)

Hendricks Community Hospital, Danville, Indiana (Nov 1984 - Mar 1988)

Emergency Physician, Midwest Medical Management, Inc. Indianapolis, Indiana (Jul 1983 - Nov 1984)

3. I received a degree in Medicine from the Indiana University of Medicine, Indianapolis, Indiana in 1980. I received a B.S. in Chemistry, Magna Cum Laude, from Indiana State University, Terre Haute, Indiana in 1977.

I completed an Internship and Residency in Internal Medicine at Methodist Hospital, Indianapolis, Indiana (1980-1983)

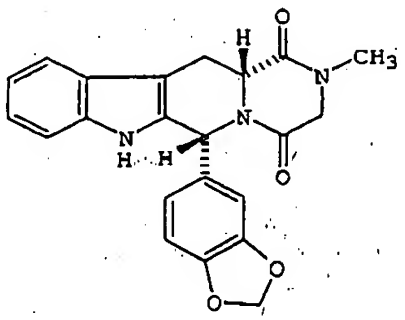
I am board certified in Internal Medicine and Emergency Medicine: Board of Certification: Diplomate, American Board of Internal Medicine, September 14, 1983 (#092096); Diplomate: American Board of Emergency Medicine, March 17, 1989 - December 31, 1999, Recertification, December 24, 1998 - December 31, 2008 (#870725)

4. I have practiced medicine for twenty three (23) years, conducted research, published about 28 articles, 4 book chapters and 35 abstracts, and presented lectures at numerous conferences, served as a member on numerous editorial boards and scientific or medical advisory boards, and have a membership in numerous societies, such as American Association of Pharmaceutical Physicians, American College of Emergency Physicians, and American College of Physicians.

5. One of my main fields of research and interest is in the field of Internal Medicine, in particular primary care product, cardiovascular, and infectious diseases.

6. I have read and understand U.S. Patent Application Serial No. 10/031,556, and I am familiar with the September 29, 2003 Office Action in the above-identified application.

7. The invention disclosed in that application is directed to a method of treating sexual dysfunction (Claims 11-17 and 20-23), including, but not limited to, male erectile dysfunction and female sexual arousal disorder, which comprises orally administering to a patient in need thereof one or more unit dose containing about 1 to about 20 mg of Compound (I), up to a maximum total dose of 20 mg per day.



(I)

8. The present invention is based on detailed experiments and clinical trials, and the unexpected discovery of a unit dosage form incorporating about 1 to about 20 mg of Compound (I) that, when orally administered, effectively treats sexual dysfunction and substantially reduces various undesirable adverse events.

9. The new and surprisingly unexpected results achieved by the present invention are illustrated in Example 7 of the specification and in an analysis of pooled data from eight subsequent Phase 3 clinical trials. Example 7 shows that compound (I) is efficacious in the treatment of erectile dysfunction at 2 mg, 5 mg, and 10 mg dosages.

10. Example 7 also shows the unexpected decrease in treatment-emergent adverse events in the table at page 32 of the specification. The results in the table of Example 7 were further corroborated in controlled Phase 3 studies. The results of an analysis of pooled data from eight Phase 3 studies for placebo, 5 mg, 10 mg, and 20 mg doses are set forth in the following table, together with the data from the table of Example 7 for placebo and the 50 mg dose. The Phase 3 studies were conducted using 20 mg or lower doses because higher doses above 20 mg of Compound (I) had a sufficient number of adverse events such that the dose would have reduced tolerability to the general public.

	Placebo [1]	Tadalafil 5 mg [1]	Tadalafil 10 mg [1]	Tadalafil 20 mg [1]	Placebo [2]	Tadalafil 50 mg [2]
Adverse Event	**(N=476)**	**(N=151)**	**(N=394)**	**(N=635)**	**(N=134)**	**(N=59)**
Headache	5%	11%	11%	15%	10%	34%
Dyspepsia	1%	4%	8%	10%	6%	20%
Back pain	3%	3%	5%	6%	5%	24%
Myalgia	1%	1%	4%	3%	3%	20%
Nasal congestion	1%	2%	3%	3%	--	--
Flushing	1%	2%	3%	3%	0%	3%
Pain in limb	1%	1%	3%	3%	--	--

(1) Data from an analysis of pooled data from eight controlled Phase 3 studies (Table 7, CIALIS US Packet Insert, Nov 2003) coded using Medical Dictionary for Regulatory Activities (version 5.0); adverse events with ≥2% incidence on tadalafil (10 or 20 mg) and more frequent on drug than placebo, and

(2) Data from table of Example 7 of specification (an analysis of data pooled from three Phase 2 studies (LVBF/DSD06, LVBG/DSD04 and LVAC); adverse events coded using the COSTART dictionary).

11. The data in paragraph 10 shows a dramatic reduction in adverse events associated with common adverse events, such as headache, dyspepsia and back pain between the 20 mg and 50 mg dosages, and further reductions for the 5 mg and 10 mg dosages. This decrease of adverse events coupled with an efficacy across the claimed dose range is an unexpected advance in the art.

12. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; further, these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or document or any patent resulting therefrom.

Gregory D. Sides, M.D.

Date: 13 Jan, 2004